REMARKS

The foregoing amendment amends claims 1 and 15 and cancels claim 23. Pending in the application are claims 1-47, of which claims 1, 15, 42 and 43 are independent. Claims 42-47 are withdrawn pursuant to a Restriction Requirement. The following comments address all stated grounds for rejection and place the presently pending claims, as identified above, in condition for allowance.

Claim 1 is amended to specify that the fluid interface port is formed in a side wall of the microchannel. Support for the amendment can be found throughout the application as originally filed, at least, for example on page 9, lines 3-6 and page 15, lines 27-30.

Claim 15 is amended to specify that the fluid interface port forms a direct interface between an interior of the microchannel and an exterior of the device. Support for the amendment can be found throughout the application as originally filed, at least, for example on page 9, lines 3-6, page 17, lines 23-26 and page 20, lines 13-17. *No new matter is added.*

Amendment and/or cancellation of the claims is not to be construed as an acquiescence to any of the objections/rejections set forth in the instant Office Action, and was done solely to expedite prosecution of the application. Applicant reserves the right to pursue the claims as originally filed, or similar claims, in this or one or more subsequent patent applications.

Supplemental Information Disclosure Statement

Applicants include herewith a Supplemental Information Disclosure Statement citing references cited during the prosecution of European patent application EP 02737579, which relates to the present application, and during the prosecution of USSN 10/028,852 filed December 21, 2001 (Attorney Docket Number: TGZ-001A) and USSN 10/027,484, filed December 21, 2001 (Attorney Docket Number: TGZ-001B), which are currently being prosecuted before the United States Patent and Trademark Office and also relate to the present application.

Claim Rejections Under 35 USC §112

Regarding the rejection of claim 23 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, Applicants maintain that the term "encapsulant" would be understood by one of ordinary skill in the art and comprises any suitable material in liquid form that may be applied over a fluid in a fluid interface port to cover and seal the fluid interface port. The encapsulant is preferably immiscible with the fluid in the microchannel. However, to expedite prosecution of the application, Applicants have canceled claim 23.

Double Patenting

Claims 15-41 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 and 58-150 of copending Application No. 10/028,852 as characterized by US 2003/0007898. Applicants submit that the claims are patentably distinct from the claims of co-pending U.S. Patent Application No. 10/028,852. If necessary, Applicants will file a terminal disclaimer to overcome the provisional double-patenting rejection.

Claim Rejections Under 35 USC §102

In the Office Action, the Examiner issues a new rejection of claims 1-41 under 35 USC §102(e) as being anticipated by the Barbera-Guillem reference. Applicants traverse the rejection and submit that the pending claims distinguish patentably over the cited references, in particular over the cited Barbera-Guillem reference.

According to the Examiner, the Barbera-Guillem reference discloses a device having a plurality of microchannels and interfaces with a volume of about one nanoliter. According to the Examiner, a "virtual wall" is an interconnecting channel having a volume of about one nanoliter. Therefore, the Examiner considers the Barbera-Guillem reference to disclose the claimed microfluidic device. Applicants respectfully disagree.

As used in the present application, a "virtual wall" is not an interconnecting channel having a volume of about one nanoliter, as alleged by the Examiner. Rather, a virtual wall refers to a particular type of *meniscus* formed in an opening of a side wall of a microchannel that is

sized and dimensioned so that the meniscus essentially replaces the removed portion of the side wall that defines the fluid interface port. A virtual wall does not refer to *any* and every type of meniscus (i.e., all menisci are not virtual walls), but rather a meniscus in an opening that is specifically sized and configured so that the fluid flow through the microchannel is not affected by the fact that a portion of the side wall of the microchannel is absent and that the microchannel is exposed to the environment (see Specification at page 17, lines 10-30).

The virtual wall forms a *direct* interface between the microchannel interior and the microchannel exterior, allowing direct access to the liquid in microchannel without introducing dead or unswept volume in the microchannel. In contrast, the filling ports 40 and the vent apertures 30 in the Barbera-Guillem reference do not *directly* interface a microchannel to the environment surrounding the device.

The virtual wall of the claimed invention also serves to seal liquid inside of the microchannel through a range of pressures in the microchannel. There is no teaching or suggestion that liquid is sealed in the device by the filling ports 40 or the vent apertures 30 of Barbera-Guillem.

A fluid interface port forming a virtual wall according to the present invention generally has a diameter of between about 0.1 μm and about 200 μm and preferably between about 25 μm and about 125 μm and most preferably between about 50 μm and about 100 μm, or another suitable cross-sectional dimension such that resulting capillary forces retain liquid within the microchannel. There is no teaching or suggestion that the filling ports 40 or the vent apertures 30 of Barbera-Guillem have such dimensions.

As set forth in independent claims 1 and 15, a virtual wall also has a relatively low dead volume, i.e., less than about one nanoliter. "Dead volume" refers to the volume of liquid retained in the fluid interface port (i.e. the volume of liquid the fluid interface port holds that is not flushed through the fluid interface port by the flow field of liquid through the microchannel). The relatively small dead volume provided by the virtual wall results in a direct fluid interface allowing direct injection of a precise volume of sample into the interior of the microchannel

from the exterior of the microchannel. The ability to directly inject sample into the microchannel due to the low dead volume of the fluid interface port provides improved control over the amount of sample that is injected into the microchannel, allows efficient use of sample, and significantly reduces waste of the sample. Furthermore, the direct injection provided by the very small dead volume reduces or prevents cross-contamination between different samples and allows a second substance to be directly injected into the system immediately after a first substance without requiring flushing of the fluid interface port. In contrast, the filling ports 40 and venting apertures 30 in the Barbera-Guillem reference have significantly larger dead volumes. For example, as recited in paragraph [0035], "each filling port comprises a passage that extends through base 12." The long length of each filling port results in a relatively large dead volume that cannot be minimized, in contrast to the claimed fluid interface port.

Applicants therefore submit that the structure of the virtual wall is sufficiently defined, and is patentably distinct from the ports disclosed in the Barbera-Guillem reference.

The Barbera-Guillem reference does not disclose a virtual wall fluid interface port formed in a side wall of a microchannel or a method of forming such a fluid interface port, as recited in independent claims 1 and 15. In fact, the Barbera-Guillem reference teaches *away* from the claimed invention.

The Barbera-Guillem reference discloses a device for performing analyses of live cells having a plurality of microchambers. The chambers do not constitute microchannels, because the chambers do not allow for fluid flow. As set forth in the specification, the term "channel" as refers to a pathway formed in or through a medium that allows for movement of fluids, and a microchannel is a channel having cross-sectional dimensions in the range between about 1.0 μm and about 250 μm. The microchambers of Barbera-Guillem do not meet these parameters. The microchamber of Barbera-Guillem has a capacity of between about 100 nanoliters and about 500 microliters, but there is no teaching or suggestion regarding the cross-sectional dimension of the microchamber.

Each micro*chamber* in the Barbera-Guillem device has an associated vent and filling port connected through *intermediate* means. There is no direct interface between a chamber and an exterior. In fact, the Barbera-Guillem reference specifically teaches *away* from a direct interface in paragraph [0038], which specifies that the filling port 40 provides "for introducing a fluid into the microchamber without direct access to the microchamber (i.e., without injecting the fluid directly into the microchamber or directly onto analyte that may be contained within the microchamber." Paragraph [0038] further describes the advantages of indirect access, such as allowing fluid to perfuse or permeate an analyte. In contrast, as described above, the use of a direct fluid interface, as set forth in the present invention, enhances control of the sample, prevents dispersion and allows for a second sample to be directly injected into a microchannel after the a first sample. Therefore, the Barbera-Guillem reference expressly teaches away from a structure for providing a direct interface between a microchannel interior and an external environment, as set forth in the claimed invention.

In addition, neither the vent aperture nor the filling port has a size that would form a virtual wall. Rather, each filling port and filling aperture comprises a long passage filled with liquid that has a volume that is much larger than one nanoliter. The mere presence of the word "microfluidics" in paragraph [028] does not imply that a fluid interface port has a dead volume of less than one nanoliter, as set forth in the claimed invention. Rather, paragraph [028] of Barbera-Guillem merely signifies that microfluidic structures provide passage to a small volume of fluid. Both the vent aperture 30 and the filling port 40 in Barbera-Guillem have significantly larger sizes that do not form a virtual wall and do not have minimal dead volume.

For at least these reasons, Applicants submit that the claims distinguish patentably over the Barbera-Guillem reference.

Claim Rejections Under 35 USC § 103

Claims 1-41 are rejected under 35 USC §103(a) as being unpatentable over Dubrow et al. alone or further in view of Barbera-Guillem. Even in combination, the cited references do not disclose the claimed invention. Specifically, the cited references fail to disclose a fluid interface port sized and configured to form a virtual wall and having a dead volume of less than one nanoliter.

As recognized by the Examiner, the Dubrow reference does not disclose a fluid interface port having a dead volume that is less than about one nanoliter. The Barbera-Guillem reference does not compensate for the deficiencies of the Dubrow reference. As described above, the Barbera-Guillem reference also does not teach or suggest a fluid interface port that forms a virtual wall, or a fluid interface port having a dead volume of less than about one nanoliter. Rather, as described above, the Barbera-Guillem reference teaches *away* from forming a virtual wall and minimizing dead volume.

The Dubrow reference also teaches *away* from minimizing the dead volume, because the principal object of the Dubrow reference is to increase the volume of a fluid input port. For example, as specifically set forth in column 8, lines 5-12, the Dubrow reference seeks to "increase the volume capacity of the reservoirs of [microfluidic] devices." As set forth on lines 20-33 of column 8, the apertures of the microfluidic device of Dubrow have larges sizes (at least one millimeter deep) and volumes of at least on microliter, which is significantly, i.e., at least one thousand times, larger than a dead volume of less than one nanoliter. The Dubrow reference clearly does not suggest decreasing the dead volume of a fluid interface port and in fact expressly teaches that it would not be desirable to do so.

Furthermore, the Examiner has not pointed to an object reason for combining the cited reference in rendering the conclusion that claims 1-41 are obvious. Therefore, the Examiner fails to make a proper *prima facie* case of obviousness.

For at least these reasons, Applicants respectfully submit that all pending examined claims are patentable, and request that the objections and rejections be reconsidered and withdrawn.

CONCLUSION

In view of the above amendment, applicants believe the pending application is in condition for allowance.

Applicants believe no fee is due with this Amendment. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. TGZ-001C from which the undersigned is authorized to draw.

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Respectfully submitted,

By _____

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